## REMARKS

### I. Claim Status

Claims 1-47 were originally filed. In response to the telephonic Restriction Requirement and Species Election of 7 December 2007, Applicants elected with traverse the invention of Group I, corresponding to claims 1-36 and 39-45. In an Office Action dated 14 January 2008, the Examiner indicated claims 17, 18, 34, 35, 37, 38, and 44-47 were withdrawn based on the restriction and species election. In an Amendment filed 14 July 2008, re-filed on 5 September 2008, Applicants amended claims 1-3, 9-11, 16, 19, 21, 22, and 28, canceled claims 6-8 and 39-45 without prejudice to their renewal, and added new claims 48 and 49. Thus, claims 1-5, 9-38, 46-49 were pending. In a Request for Continued Examination dated 6 July 2009, Applicants amended claims 1, 10, and 11, and canceled claims 2-5 without prejudice. Thus, claims 1, 9-38, and 46-49 were pending. In an Amendment dated 22 March 2010, Applicants amended claims 1, 12, 13, 16, 27-31, and 36, and canceled claims 9-11, 17-26, 34-35, 37-38, and 46-47 without prejudice. Thus, claims 1, 12-16, 27-33, 36, 48, and 49 were pending. In a Request for Continued Examination dated 9 December 2010, Applicants amended claims 1, 13, 14, 15, 16, 48, and 49, and canceled claims 27-33 and 36 without prejudice. Thus, claims 1, 12-16, 48, and 49 were pending and were the subject of the present Office Action.

Claims 1 and 49 are amended herein, and claim 48 is canceled without prejudice. Accordingly, claims 1, 12-16, and 49 are pending. Support for amended claim 1 can be found throughout the specification, for example, at paragraph [0038], and in claim 48, which is canceled herein. Amendment to claim 49 merely corrects claim dependency. No new matter is introduced by any of these amendments, and entry of the amendments is respectfully requested.

### II. Rejections under 35 U.S.C. §102

The Examiner maintained the rejection of claims 1, 12-13, 15-16, 48 and 49 under 35 U.S.C. 102(e) as being anticipated by Klaus et al., U.S. Patent Application Publication 2003/0153503, as newly evidenced by Skarpidi et al. (2003) Experimental Hematology 31:197-203, cited previously. The Examiner stated that "[t]he claims are drawn to a method for treating hemoglobinopathy in a subject," and that "Klaus et al teaches the same active method steps . . . in order to treat a hemoglobinopathy." (Office Action, page 4.)

The Examiner further stated that

> as evidenced by Skarpidi et al . . . one of skill would have recognized that the hydroxamate iron chelators (which are inhibitor [sic] of hypoxia inducible factor prolyl hydroxylase as taught by Klaus et al) have the inherent property of being able to increase the level of fetal hemoglobin as well as increase the expression of the gene encoding γ-globin . . . .

(Office Action, page 4.) Following consideration of Applicants' argument filed 9 December 2010, the Examiner reiterated that "Klaus et al discloses the same HIF prolyl hydroxylase inhibitors as claimed for treating the same condition in the claims, i.e., hemoglobinopathy." As claim 48 is canceled above, the rejection is moot as applied to this claim. With respect to claims 1, 12-13, 15-16, and 49, Applicants respectfully traverse.

Applicants have amended claim 1 above. As amended, claim 1 recites in relevant part "[a] method for treating a hemoglobinopathy in a subject, the method comprising administering to the subject in need thereof a compound that inhibits hypoxia-inducible factor (HIF) prolyl hydroxylase, wherein the compound is a structural mimetic of 2-oxoglutarate . . . ." As the amended claims do not recite "hydroxamate iron chelators," Skarpidi et al. are not relevant to the claimed subject matter.

Claim 1 and claims 12-13, 15-16, and 49 which depend directly or indirectly from claim 1 recite methods for "treating a hemoglobinopathy in a subject." The issue therefore is whether methods for treating a hemoglobinopathy in a subject are anticipated by Klaus et al. under 35 U.S.C. §102(e).

Section 102(e) recites in relevant part "a person shall be entitled to a patent unless . . . the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent . . . ." 35 U.S.C. §102(e). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); also see, Manual of Patent Examining Procedure (MPEP) § 2131 (8th Ed., latest revision July 2010). "To anticipate, the reference 'must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements 'arranged as in the claim''. . . (The reference must clearly and unequivocally disclose the claimed [invention] or direct those skilled in the art to the [invention] without *any* need for picking, choosing, or combining various disclosures not directly related to each other by the teachings of the cited reference." *Sanofi-Synthelabo v. Apotex, Inc.*, 90 U.S.P.Q.2d 1370, 1375 (Fed. Cir. 2008), cert. denied, 130 S. Ct. 493 (2009) (Emphasis in original).

The present rejection rests on the allegation that Klaus et al. "teach a method for treating hemoglobinopathy in a subject" as presently claimed. The Examiner contends that "Klaus et al discloses the same HIF prolyl hydroxylase inhibitors as claimed for treating the same condition in the claims, i.e., hemoglobinopathy." The only citation in Klaus et al. provided by the Examiner to evidence this contention (paragraph 80) recites various conditions, diseases, and disorders that may be associated with anemia. Klaus et al. do not recite "a method for treating a hemoglobinopathy in a subject." As Klaus et al. do not recite a method for treating a hemoglobinopathy, Klaus et al. do not set forth explicitly or inherently each and every element in the present claims. Skarpidi et al. provide no evidence to the contrary. Therefore, Klaus et al. do not anticipate claims 1, 12-13, 15-16, and 49.

For at least the reasons provided above, claims 1, 12-13, 15-16, and 49 are not explicitly or inherently anticipated by Klaus et al., and Applicants respectfully request withdrawal of the rejection of these claims under 35 U.S.C. §102(e) as being anticipated by this reference.

## III. Rejections under 35 U.S.C. §103

The Examiner maintained the rejection of claims 1, 12-16, and 48-49 under 35 U.S.C. 103(a) as being anticipated by Klaus et al., U.S. Patent Application Publication 2003/0153503, in view of Perrine et al., International Publication No. WO 93/18761, as newly evidenced by Skarpidi et al. (2003) Experimental Hematology 31:197-203, cited previously. The Examiner stated that "Klaus et al teach that hemoglobinopathy such as abnormal hemoglobin such as beta thalassemia can be treated by administering HIF prolyl hydroxylase inhibitors such as hydroxamate or structural mimetics of 2 oxo-glutarate," and "Perrine et al teach other types of β thalassemia such as $\beta^o$- or $\beta^+$-thalassemia." (Office Action, page 8-9.) The Examiner stated that "as evidenced by Skarpidi et al . . . one of skill in the art would have recognized that the hydroxamate iron chelators . . . have the inherent property of being able to increase the level of fetal hemoglobin as well as increase the expression of the gene encoding γ-globin . . . ." (Office Action, page 8.) The Examiner contends that "[i]t would have been prima facie obvious to one of ordinary skill in the art to have used the method of Klaus et al to treat other β thalassemia disorders such as $\beta^o$- or $\beta^+$-, thus resulting in the instant invention with a reasonable expectation of success" (Office Action, page 8.) As claim 48 is canceled above, the rejection is moot as applied to this claim. With respect to claims 1, 12-16, and 49, Applicants respectfully traverse.

As stated above, Applicants have amended claim 1, which presently recites in relevant part "[a] method for treating a hemoglobinopathy in a subject, the method comprising administering to the subject in need thereof a compound that inhibits hypoxia-inducible factor (HIF) prolyl hydroxylase, wherein the compound is a structural mimetic of 2-oxoglutarate . . . ." Therefore, the question is whether it would have been obvious to one of skill in the art to use the methods of Klaus et al. to treat a hemoglobinopathy in a subject as presently claimed in view of the teachings of Perrine et al. with respect to $\beta^0$- and $\beta^+$-thalassemia.

Section 103 provides in relevant part that "a patent may not be obtained, though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a). Obviousness is a question of law based on underlying factual inquiries, which were enunciated by the Court as follows: (A) identifying the scope and content of the prior art; (B) ascertaining the differences between the claimed invention and the prior art; and (C) resolving the level of ordinary skill in the pertinent art." *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). The *Graham* factors were reaffirmed and relied upon by the Supreme Court in its consideration and determination of obviousness in the fact situation presented in *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007).

The present invention provides methods "for treating a hemoglobinopathy in a subject." The Examiner cites Klaus et al. and Perrine et al. as prior art relevant to the patentability of the invention. The Examiner characterizes Klaus et al. as disclosing "the same HIF prolyl hydroxylase inhibitors as claimed for treating the same condition in the claim i.e. hemoglobinopathy." (Office Action, page 9.) However, as argued above, Klaus et al. does not recite methods for treating hemoglobinopathy in a subject. Therefore, for the present claims to be obvious in view of Klaus et al., Perrine et al. would have to provide some teaching or suggestion to use the methods of Klaus et al. to treat hemoglobinopathy in a subject. Perrine et al. does not provide this link. Therefore, the present claims are not obvious based on the teachings of Klaus et al. when considered alone or in view of Perrine et al.

As the amended claims do not recite "hydroxamate iron chelators," Skarpidi et al. are not relevant to the claimed subject matter.

For at least the reasons provided above, claims 1, 12-16, and 49 are nonobvious over Klaus et al. and Perrine et al., and Applicants respectfully request withdrawal of the rejection of these claims under 35 U.S.C. §103(a) as being unpatentable over these references.

## CONCLUSION

In view of the foregoing, Applicants submit that the claims are fully in condition for allowance and request early notification to that effect.

**Applicants claim small entity status under 37 C.F.R. 1.27.**

The Commissioner is hereby authorized to charge the total of the fees due in this communication to Deposit Account No. 50-0811, referencing Docket No. FP0617 US.

Please call Applicants' representative at 415-978-1745 with any questions regarding the present communication or the above-identified application.

Respectfully submitted,

Date: 1 Aug. 2011 By: _____

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